Comorbid Chronic Tic Disorder and Tourette Syndrome in Children Requiring Inpatient Mental Health Treatment

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Key words

Tourette, tics, children, inpatient admission, mental health

Conflict of interest

SZ, RL, EP, DD and MK report no conflict of interest related to this work.

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Abstract

Objective: Children needing admission to an inpatient mental health unit often present with severe neuropsychiatric disorders characterised by complex psychopathology. We aimed to examine all admitted children with comorbid chronic tic disorder (CTD) and Tourette syndrome (TS) over a 10-year period and determine the clinical significance of these diagnoses.

Method: A retrospective, naturalistic study was conducted, comparing children with and without CTD/TS in terms of co-morbid diagnoses, medication use, access to education, aggression contributing to the admission, duration of admission, functional outcomes, and satisfaction with treatment. Data were analysed using Chi-square/Fisher's exact test and t-test for categorical and continuous variables, respectively, and subsequently with unadjusted and adjusted linear and logistic regression analyses.

Results: A relatively high proportion of children had co-morbid CTD/TS (19.7%). There was a significant association with co-morbid obsessive-compulsive disorder, intellectual disability and autism spectrum disorder but not attention deficit hyperactivity disorder. CTD/TS were associated with longer admissions even after adjustments for confounding but did not seem to be independently associated with other examined clinical characteristics.

Conclusions: The prevalence of CTD/TS in children needing inpatient treatment is significant. In our sample, comorbid CTD/TS seem to represent a marker of overall symptom severity as evidenced by longer admissions.

Introduction

Children in need of admission to an inpatient mental health unit often present with severe neuropsychiatric disorders characterised by complex psychopathology in multiple domains (Kyriakopoulos et al, 2015; Green et al 2007). Among their symptoms, admitted children occasionally present with comorbid tic disorders, a group of phenomenologically heterogeneous neuropsychiatric conditions that involve rapid, repetitive, involuntary movements or vocalisations (Efron and Dale, 2018). Of these, Tourette syndrome (TS) is the most severe and extensively researched. TS is characterised by the presence of both motor and vocal tics, for a period of at least one year without periods of tic remission lasting more than two months (World Health Organization, 2018). Motor tics include simple movements such as eye blinking, facial grimacing, arm, trunk, or leg movements, or more complex whole-body movements, including inappropriate gestures (copropraxia). Vocal tics include simple noises such as throat clearing, humming, sniffing, squeaking or more complex vocalisations including words, repeating phrases, or even swear words (coprolalia) (Leckman, 2003). The prevalence of TS is estimated at 0.3-0.8% of school age children (Scahill et al., 2005; Hirtz et al., 2007) and has been associated with a wide range of neurodevelopmental and mental health conditions including attention deficit hyperactivity disorder (ADHD), autism spectrum disorders (ASD), obsessive compulsive disorder (OCD) and other anxiety disorders, as well as challenging behaviours and aggressive outbursts (Swain et al, 2007). Hirschtritt and colleagues (2015) found that the estimated lifetime prevalence of any psychiatric comorbidity in TS is 85.7%. Alongside TS, chronic motor or vocal tic disorder (CTD) is characterised by the same tic duration criteria but tics are either motor or vocal, not

both. CTD is more common than TS with an estimated prevalence of 0.5 – 1.1% (Scharf et al, 2012) but less researched in terms of its associated psychopathology. The severity of tics can range from mild, which can occur without much apparent consequence to the child's overall psychopathology, to severe which are disabling and affect all aspects of functioning, requiring specific interventions in their own right (Leckman et al, 1989). In mixed neurodevelopmental presentations, tics, especially when mild in intensity, may not always be considered as a significant factor in the decision-making process of the child's treatment and overall management (Ernberg et al, 1987; Storch et al, 2007). Indeed, there is no evidence to recommend that the treatment of comorbid developmental disorders should differ between those with and without tics (Bloch and Leckman, 2009).

The main symptomatology of children with severe disorders needing inpatient treatment is not commonly identified as being directly linked with comorbid TS or CTD. As such, the relative significance of the presence of tics in these children has not been studied to date. The aim of this study was to examine the demographic and clinical characteristics of children with comorbid CTD/TS up to the age of 12 years admitted to a children's inpatient mental health unit, and to evaluate the clinical significance of CTD/TS on their overall treatment, educational and functional outcomes, duration of admission, and satisfaction with the input they received. We hypothesised that comorbid CTD/TS would be associated with higher illness burden, lengthier admissions, and higher levels of associated aggression compared to children without these conditions.

Methods

A retrospective naturalistic study was conducted of all patients discharged from a national inpatient children's mental health unit between the years 2009 to 2019 during their admission. The unit provides inpatient assessment and treatment for children aged up to 13 years with severe and complex disorders. These include children with neuropsychiatric disorders such as autism spectrum disorders (ASD) and attention deficit hyperactivity disorder (ADHD), depression, very early onset psychosis and bipolar affective disorder, obsessive-compulsive disorder, eating disorders, stress-related disorders, and complicated diagnostic conditions. The service is one of only eight child inpatient units in England and Wales. More information about this can be found in a previous publication (Kyriakopoulos et al, 2015).

Children with comorbid Chronic Tic disorder or Tourette syndrome (CTT group) were identified and compared with the remaining children (No chronic Tic disorder or Tourette syndrome: NTT group) in terms of age, gender, medication on admission and discharge, whether they were in education on admission and discharge, whether aggression, as reported in the referral information and history from families, contributed towards their admission, duration of admission, functional outcomes, and satisfaction with treatment. Tics and their duration were identified through clinical observations recorded in the electronic notes system and history from the child's family included in clinical reports. If criteria for the diagnoses of CTD or TS were met, the child was included in the CTT group. The CGAS (Children's Global Assessment

Scale) on admission and at discharge was used to assess global functioning (Shaffer et al, 1983). It takes values from 1, representing the lowest level of functioning, to 100, representing the highest. This scale was recorded by the unit's team in a way that was blinded to the purpose of the current study. Not being in education was defined as not attending school for more than 50% of the time for at least two weeks prior to admission or not having an educational setting identified at discharge. Diagnoses were made in accordance with the Multiaxial ICD-10 classification of child and adolescent psychiatric disorders (World Health Organization, 1996) and the ICD-10 diagnostic criteria for research (World Health Organization, 1993), and additional diagnostic assessments as appropriate, including the Autism diagnostic observation schedule (ADOS; Lord et al, 1989), the Autism Diagnostic Interview-Revised (ADI-R; Lord et al, 1994), and Conners questionnaires (Conners et al, 1998). Children and parent/carer satisfaction were measured using the Acorn Satisfaction Questionnaire (ASQ) at discharge. The ASQ is a 9-item self-report measure (7 items for parents/carers and 2 items for children) which has been previously used with children with mental health difficulties requiring inpatient admission (Kyriakopoulos et al., 2015). Each item is rated on a Likert scale from 1 to 5, with higher scores indicating higher satisfaction.

Statistical analysis

Data were analysed initially using Chi-square/Fisher's exact test and t-tests for categorical and continuous variables, respectively. CTT and NTT were also compared in terms of their comorbid diagnoses to determine the likelihood of

comorbidity with tics. ADHD, OCD, ASD, intellectual disability (ID), and aggression were specifically examined. Next, a series of unadjusted (Model A) and multiple regression analyses (Model B) were performed to examine the associations between the CTT group and all sociodemographic and clinical characteristics before and after adjustments for confounding. The NTT group served as the reference category in all regression models. Covariates in Model B included age, gender, and comorbid disorders including ID, ASD, ADHD, and OCD. Linear regression analyses were performed for continuous outcome variables (functional outcomes at admission and discharge, child and parent/carer satisfaction, and duration of treatment) and logistic regression analyses for binary outcomes (medication at admission and discharge, education on admission and discharge, and presenting with aggression on admission). The regression coefficients were accordingly expressed as unstandardised beta (β) values or Odds ratios (OR). Analyses were performed using the IBM Statistical Package for Social Sciences (SPSS) version 26.0 and Stata/MP 16.1.

This study was part of a service evaluation project which was approved by the South London and Maudsley NHS Foundation Trust Child and Adolescent Mental Health Services Clinical Academic Group Clinical Governance/Audit Committee.

Results

During the study period, a total of 218 children were discharged from our unit (45.9% female) and their admission data were included in this analysis. Forty-three patients were in the CTT group (19.7%) and 175 were in the NTT group (80.3%). CTT compared to NTT were more likely to be male at a trend level ($\chi^2 = 3.824$, df = 1, p = 0.051), receive medication on admission ($\chi^2 = 5.655$, df = 1, p = 0.017) and at discharge ($\chi^2 = 6.106$, df = 1, p = 0.013), present with aggression contributing to their admission ($\chi^2 = 4.944$, df = 1, p = 0.026) and have longer admission (t = -2.763, p = 0.008). No significant differences were found between the CTT group and NTT group in terms of age on admission (t = 0.35, p = 0.727), education on admission ($\chi^2 = 1.261$, df = 1, p = 0.262), education at discharge (Fisher's exact test p = 1.0), mean CGAS score on admission (t = 0.981, p = 0.328) and at discharge (t = 1.374, p = 0.171), mean CGAS score change (t = 0 .491, p = 0.624), parent/carer satisfaction (t = 0.454, df = 187, p = 0.65) or child satisfaction with treatment (t = -0.651, df = 166, p = 0.516). Table 1 summarises the demographic and clinical characteristics examined.

In the CTT group, 81.4% of children (35/43) had a comorbid ASD diagnosis compared with 48% (84/175) in the NTT group ($\chi^2 = 15.529$, df = 1, p > 0.001), 30.2% (13/43) had a diagnosis of ADHD compared with 25.1% (44/175) in the NTT group ($\chi^2 = 0.463$, df = 1, p = 0.496), 27.9% (12/43) had a diagnosis of OCD compared with 12.6% (22/175) in the NTT group ($\chi^2 = 6.167$, df = 1, p = 0.013), and 30.2% (13/43) had a comorbid diagnosis of ID compared with 10.6% (19/175) in the NTT group ($\chi^2 = 10.347$, df = 1, p = 0.001). Table 2 summarises the results below.

Tables 3 and 4 summarise the results of the continuous and logistic regression models, respectively. Of the significant associations in the unadjusted linear regression model between CTT group membership and medication on admission and at discharge, aggression contributing to admission, and duration of admission, only the relationship with duration of admission remained statistically significant in the adjusted linear regression models (β=51.34, $p<.01$). The significant bivariate associations between CTT group membership and the remaining outcomes were explained by presence of comorbid diagnoses. Specifically, a diagnosis of ADHD was associated with increased odds for receiving medication on admission (OR=6.34, 95%CI 2.69-14.94) and discharge (OR=8.73, 95%CI 1.85-41.15), and presenting with aggression prior to admission (OR=6.38, 95%CI 1.81-22.54). A diagnosis of ASD was associated with increased odds for receiving medication on discharge (OR=3.45, 95%CI 1.49-7.99) and for having aggression contributing to admission (OR=2.38, 95%CI 1.14-4.95).

Discussion

In this naturalistic study, we systematically examined during their admission all children discharged from a national children's inpatient mental health unit over a ten-year period. Given the unique sample of patients admitted, we expected and noted that our sample had a relatively high proportion of children with comorbid CTD/TS (19.7%), as compared with the general population where population prevalence of TS and CTD is 0.3-0.8% and 0.5-1.1 respectively (Scharf et al, 2012). Our interest was in closely examining this group of children to determine the clinical correlates

and characteristics associated with the prevalence of CTD/TS, and to determine whether these conditions impacted on their overall functioning and morbidity.

Clinical profile of children with CTD/TS

Children with CTD/TS displayed greater neurodevelopmental deviance as was demonstrated by the significant association with a comorbid ASD, OCD, and ID. This is in keeping with previous studies; Robertson (2000) noted a strong association between OCD and TS, reporting that up to 40% of patients with TS report comorbid obsessive-compulsive symptoms and behaviours. OCD has been identified as one of the most frequent comorbidities in TS with its prevalence ranging from 10% to 66% in this group of patients (Cravedi et al., 2017; Hirschtritt et al, 2015; Sambrani et al, 2016). In our sample, the prevalence of comorbid OCD with CTD/TS was 27.9%, similar to recent findings from Gorman and colleagues (2010) at 25% and Eapen and colleagues (2016) at 35%. Studies have also consistently shown an association between TS and ID. Estimates vary from as little as 5.4% (Byler et al, 2015) to 24-27% (Eapen et al, 2016, Gorman et al 2010). An analysis of 5450 subjects in the 'TIC' database (Burd et al, 2005) estimated a 22.7% prevalence of ID. These are broadly consistent with our findings, though notably we found a higher prevalence of comorbid CTD/TS with ID, at 30.2%, in children requiring hospital admission.

It is of note that in our cohort the prevalence of ASD in CTD/TS was 81.4% which is significantly higher than in outpatient samples. Two large clinical cohorts of TS patients and their families were screened for the presence of ASD symptoms and

identified a ‘probable’ incidence of ASD of about 20% in this group (Darrow et al, 2017; Huisman-van Dijk et al, 2016). A recent study by Eapen and colleagues (2016) in subjects with an established diagnosis of TS who were asked to report on established comorbid diagnoses found that ASD was reported in 21% of children. This is higher than previous incidence reports ranging from 2.9% to 4.9% in clinical populations (Burd et al, 2009 and Ghanizadeh and Mosallaei, 2008). The large difference between our sample and outpatient samples may reflect the fact that children with ASD needing inpatient input are more likely to present with more severe symptoms and multiple comorbidities, frequently including chronic tics and TS.

Interestingly, we did not find a significant association between CTD/TS and ADHD. Research into TS and ADHD has shown frequent co-occurrence of the two disorders, with studies suggesting comorbidity rates ranging between 21 to 90% in studied cohorts (Robertson, 2006). Oluwabusi and colleagues (2016) also found that between 35-90% of children with TS present with ADHD symptoms. A meta-analysis of genome-wide association studies of ADHD and TS has found evidence of a common genetic background and that specific genes may underlie both disorders (Tsetsos et al, 2016). One possible reason why our study did not pick up this association may be related to the relatively low proportion of patients admitted to our ward with ADHD (26%).

The presence of CTD/TS was also significantly associated with aggression in our sample. However, this relationship seems to be driven by comorbid ADHD and ASD

rather than being a direct effect of tics. A complex interplay of aetiological factors is believed to contribute to aggression in TS, including genetic, neurobiological and environmental factors (Budman, 2015). The majority of studies examining the association between TS and aggression, support a link between the two (Ghanizadeh & Mosallaei, 2009, Cavanna et al 2014; Wright et al, 2012). One study that compared children with TS-alone to those with TS with comorbidity suggested that aggression is related to the increase symptom burden associated with comorbidity rather than tics (Benaroya-Milshtein et al, 2020). A diagnosis of TS and comorbid ADHD is thought to be strongly associated with aggression, again supporting the notion that it is the comorbidity that is associated with aggression rather than the presence of CTD/TS (Budman et al, 2015). However, another study suggested a more direct relationship between tic severity and aggression (Robertson et al, 2015). Further research including larger samples may shed more light into the possibility of tics independently contributing to aggressive behaviours when comorbid with other neurodevelopmental or mental health conditions.

Children with comorbid CTD and TS had similar gains in global functioning to children without these presentations during their admission but stayed in hospital for longer. Satisfaction with treatment also seems not to be independently associated with comorbid CTD and TS despite the need for additional treatment and may reflect this level of overall improvement. However, longer admissions suggest an additional symptom burden and need for more extended interventions to achieve the same functional outcomes in this group. The literature into the association between CTD/TS and functional impairment is inconclusive. In some studies, TS has been associated with significantly worse quality of life outcomes than the general

population, particularly in the adult literature (Eddy et al, 2011; Elstner et al, 2001) and research to date indicates that severe forms of TS may impact on home, school/work life, education, gaining independence and relationships with family and friends (Eapen et al 2016). However, other studies have suggested that the impairment may be due to comorbidities, rather than tics alone (Coffey et al, 2004, Robertson et al, 2015). One study comparing TS patients with comorbidities to those without have shown that those with TS with comorbidities, particularly ADHD, exhibit higher levels of cognitive and behavioural disability than children with TS alone (Rizzo et al, 2007). Other studies have noted that patients with TS with comorbidity did not necessarily exhibit greater tic severity and that tic severity was not associated with a greater number of comorbidities (Specht et al, 2011). This suggests a more complex relationship exists between the presence of tics, comorbidities and resulting impairment.

Strengths and Limitations

A considerable strength of our study is the that our sample spans ten years and offers an insight into the demographics and clinical characteristics of this unique population of young children requiring inpatient care. Limitations include the relatively small sample size, and the retrospective nature of our investigation which did not allow for the prospective quantification of the severity and impact of tics with the use of a validated scale. Although selection bias is one of the limitations of retrospective studies, we feel it is less likely in our investigation as tics were

evaluated independently of the children's comorbid diagnoses which were recorded at the point of discharge.

Conclusions

The prevalence of CTD/TS in children needing inpatient treatment is significant. In our sample, comorbid CTD/TS seem to represent a marker of overall symptom severity as is evidenced by longer hospital admissions. CTD/TS did not seem to be independently associated with medication use, aggression contributing to the children's admission, functional outcomes, or satisfaction with treatment after adjustments for comorbid disorders. This may suggest that the additional clinical burden of these tic disorders in children requiring mental health hospitalisation is manifested by their need to receive longer treatment to achieve similar benefits.

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Table 1. Demographic and clinical characteristics of children with Chronic Tic Disorder or Tourette syndrome (CTT) and without (No chronic Tic disorder or Tourette syndrome: NTT)

	CTT N = 43 (19.7%)	NTT N = 175 (80.3%)	p value
Female (%)	14 (32.5)	86 (49.1)	0.051
Mean age in years (SD)	10.7 (1.6)	10.8 (1.7)	0.350
Medication on admission N (%)	31 (72.1)	91 (52)	0.017*
Medication on discharge N (%)	40 (93)	133 (76)	0.013*
Not in education on admission N (%)	21 (48.8)	69 (39.4)	0.262
Not in education on discharge N (%)	2 (4.7)	9 (5.1)	1.0
Aggression contributed to admission N (%)	37 (86)	121 (69.1)	0.026*
Mean length of admission in days (SD)	207.3 (166.4)	135.1 (83.7)	0.008**
CGAS on admission mean score (SD)	25.3 (12.6)	27.5 (13.3)	0.328
CGAS on discharge mean score (SD)	54.4 (12.6)	58.1 (16.7)	0.171
CGAS change mean score (SD)	29.1 (17.6)	30.7 (19.7)	0.624
Satisfaction Child*** - ASQ mean score (SD)	7.9 (5.3)	7.5 (2.5)	0.663
Satisfaction Parent/Carer*** - ASQ mean score (SD)	30 (6.2)	30.5 (5.1)	0.65

N: Number of children, ASQ: Acorn Satisfaction Questionnaire

* $p<0.05$, ** $p<0.01$

*** ASQ data was available in the CTT group for 35 children (81.4%) and 36 parents/carers (83.7%) and in the NTT group for 133 children (76%) and 153 parents/carers (87.4%). All other data is complete.

Table 2. Co-morbid diagnoses in children with Chronic Tic Disorder or Tourette syndrome (CTT) and without (No chronic Tic disorder or Tourette syndrome: NTT)

	CTT N = 43 (19.7%)	NTT N = 175 (80.3%)	p value
ASD (%)	35 (81.4)	84 (48)	>0.001**
ADHD (%)	13 (30.2)	44 (25.1)	0.496
OCD (%)	12 (27.9)	22 (12.6)	0.013*
ID (%)	13 (30.2)	19 (10.6)	0.001**

ASD: autism spectrum disorder, ADHD: attention deficit hyperactivity disorder, OCD: obsessive compulsive disorder, ID: intellectual disability.

* $p<0.05$

** $p<0.01$

Table 3. Crude and adjusted unstandardised regression coefficients (SE) of linear regression models examining the associations between chronic tic disorder/Tourette syndrome (CTD/TS) with demographic and clinical characteristics

	CGAS on admission		**CGAS on discharge**		**Child Satisfaction**		**Parent/Carer Satisfaction**		**Duration of admission**	
	Model A beta (SE)	*Model B beta (SE)*	*Model A beta (SE)*	*Model B beta (SE)*	*Model A beta (SE)*	*Model B beta (SE)*	*Model A beta (SE)*	*Model B beta (SE)*	*Model A beta (SE)*	*Model B beta (SE)*
With CTD/TS	-2.19 (2.24)	-2.35 (2.44)	-3.75 (2.73)	2.48 (2.61)	0.40 (0.62)	0.01 (0.67)	-0.45 (0.98)	0.33 (1.04)	72.26 (17.88)**	51.34 (18.96)**
Age	---	0.03 (0.05)	---	-1.00 (0.05)	---	-0.01 (0.01)	---	-0.03 (0.02)	---	-0.47 (0.38)
Female	---	1.44 (1.95)	---	3.65 (2.08)	---	-0.74 (0.53)	---	-1.26 (0.81)	---	3.31 (15.13)
ID	---	-0.72 (2.67)	---	-7.78 (2.85)**	---	1.18 (0.74)	---	-1.26 (1.11)	---	14.08 (20.72)

ASD	---	0.32 (2.04)	---	-11.20 (2.18)**	---	-0.33 (0.59)	---	-2.29 (0.85)**	---	48.49 (15.88)**
ADHD	---	2.65 (2.27)	---	-5.24 (2.43)*	---	-0.68 (0.64)	---	-0.34 (0.97)	---	-46.87 (17.68)**
OCD	---	2.13 (2.57)	---	-1.49 (2.74)	---	1.18 (0.68)	---	-0.23 (1.05)	---	28.58 (19.94)

**p<.05*

***p<.001*

Model A: Unadjusted coefficients

Model B: Adjustments for age, gender, and diagnosis of ID, ASD, ADHD or OCD

ADHD: Attention deficit hyperactivity disorder; ASD: Autism spectrum disorder; CTD/TS: chronic tic disorder/Tourette syndrome; ID: Intellectual disability; OCD: Obsessive compulsive disorder

Table 4. Crude and adjusted unstandardised odds ratios (OR; 95% CI) of logistic regression models examining the associations between chronic tic disorder/Tourette syndrome (CTD/TS) with demographic and clinical characteristics

	Medication on admission		**Medication on discharge**		**Aggression**		**In education on admission**		**In education on discharge**	
	Model A OR (95%CI)	*Model B OR (95%CI)*	*Model A OR (95%CI)*	*Model B OR (95%CI)*	*Model A OR (95%CI)*	*Model B OR (95%CI)*	*Model A OR (95%CI)*	*Model B OR (95%CI)*	*Model A OR (95%CI)*	*Model B OR (95%CI)*
With CTD/TS	2.38 (1.15-4.95)*	2.16 (0.94-4.96)	4.21 (1.24-14.31)*	2.47 (0.66-9.29)	2.75 (1.10-6.91)*	1.75 (0.62-4.94)	0.68 (0.35-1.33)	0.86 (0.41-1.81)	1.11 (0.23-5.34)	1.14 (0.21-6.26)
Age	---	1.00 (0.98-1.01)	---	1.01 (0.98-1.03)	---	0.99 (0.97-1.01)	---	0.99 (0.98-1.01)	---	0.97 (0.93-1.00)
Female	---	1.04	---	1.24	---	0.68	---	1.59	---	1.48

		(0.55-1.96)		(0.56-2.75)		(0.33-1.38)		(0.87-2.92)		(0.36-6.01)
ID	---	1.86 (0.77-4.49)	---	2.27 (0.60-8.64)	---	1.78 (0.60-5.31)	---	1.15 (0.51-2.62)	---	2.25 (0.25-20.48)
ASD	---	1.04 (0.54-1.99)	---	3.45 (1.49-7.99)**	---	2.38 (1.14-4.95)*	---	0.60 (0.32-1.13)	---	1.07 (0.26-4.50)
ADHD	---	6.34 (2.69-14.94)**	---	8.73 (1.85-41.15)**	---	6.38 (1.81-22.54)**	---	2.12 (1.03-4.36)*	---	0.19 (0.05-0.74)*
OCD	---	0.96 (0.42-2.20)	---	1.82 (0.60-5.51)	---	0.85 (0.34-2.09)	---	0.63 (0.29-1.37)	---	0.86 (0.16-4.69)

*p<.05

**p<.001

Model A: Unadjusted coefficients

Model B: Adjustments for age, gender, and diagnosis of ID, ASD, ADHD or OCD

ADHD: Attention deficit hyperactivity disorder; ASD: Autism spectrum disorder; CTD/TS: chronic tic disorder/Tourette syndrome; ID: Intellectual disability; OCD: Obsessive compulsive disorder; OR: Odds Ratio